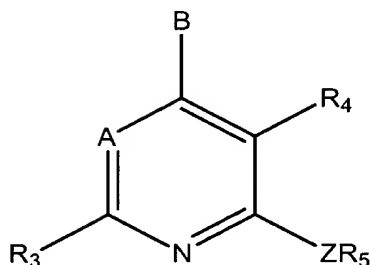


IN THE CLAIMS:

Claim 1 (Twice Amended). A compound of the formula



or a pharmaceutically acceptable salt thereof, wherein

A is -CR<sub>7</sub>;

B is -NR<sub>1</sub>R<sub>2</sub>, -CR<sub>1</sub>R<sub>2</sub>R<sub>11</sub>, -C(=CR<sub>2</sub>R<sub>12</sub>)R<sub>1</sub>, -NHCHR<sub>1</sub>R<sub>2</sub>, -OCHR<sub>1</sub>R<sub>2</sub>, -SCHR<sub>1</sub>R<sub>2</sub>, -CHR<sub>2</sub>OR<sub>1</sub>, -CHR<sub>1</sub>OR<sub>2</sub>, -CHR<sub>2</sub>SR<sub>1</sub>, ~~-C(S)R<sub>2</sub>~~, ~~-C(O)R<sub>2</sub>~~, -CHR<sub>2</sub>NR<sub>1</sub>R<sub>2</sub>, -CHR<sub>1</sub>NHR<sub>2</sub>, -CHR<sub>1</sub>N(CH<sub>3</sub>)R<sub>2</sub>, or -NR<sub>12</sub>NR<sub>1</sub>R<sub>2</sub>;

Z is NH, O, S, -N (C<sub>1</sub>-C<sub>2</sub> alkyl)-, -N(C(O)CF<sub>3</sub>), - or -C(R<sub>13</sub>R<sub>14</sub>)-,

wherein R<sub>13</sub> and R<sub>14</sub> are each, independently, hydrogen, trifluoromethyl or methyl, or one of R<sub>13</sub> and R<sub>14</sub> is cyano and the other is hydrogen or methyl, or -C(R<sub>13</sub>R<sub>14</sub>) is a cyclopropyl group, or Z is nitrogen or CH and forms a five or six membered heterocyclic ring fused with R<sub>5</sub>, which ring optionally comprises two or three further hetero members selected independently from oxygen, nitrogen, NR<sub>12</sub>, and S(O)<sub>m</sub>, and optionally comprises from one to three double bonds, and is optionally substituted with halo, C<sub>1</sub>-C<sub>4</sub> alkyl, -O(C<sub>1</sub>-C<sub>4</sub> alkyl), NH<sub>2</sub>, NHCH<sub>3</sub>, N(CH<sub>3</sub>)<sub>2</sub>, CF<sub>3</sub>, or OCF<sub>3</sub>, with the proviso that said ring does not contain any -S-S-, -S-O-, -N-S-, or -O-O- bonds, and does not comprise more than two oxygen or S(O)<sub>m</sub> heterologous members;



$R_1$  is C(O)H, C(O)(C<sub>1</sub>-C<sub>6</sub> hydrocarbyl), C(O)(C<sub>1</sub>-C<sub>6</sub> hydrocarbylene)(C<sub>3</sub>-C<sub>8</sub> cyclohydrocarbyl), C(O)(C<sub>3</sub>-C<sub>8</sub> cyclohydrocarbylene)(C<sub>3</sub>-C<sub>8</sub> cyclohydrocarbyl), C(O)(C<sub>1</sub>-C<sub>6</sub> hydrocarbylene)(C<sub>4</sub>-C<sub>8</sub> heterocyclohydrocarbyl), -C(O)(C<sub>3</sub>-C<sub>8</sub> cyclohydrocarbylene)(C<sub>4</sub>-C<sub>8</sub> heterocyclohydrocarbyl), C<sub>1</sub>-C<sub>6</sub> hydrocarbyl, C<sub>3</sub>-C<sub>8</sub> cyclohydrocarbyl, C<sub>4</sub>-C<sub>8</sub> heterocyclohydrocarbyl, -(C<sub>1</sub>-C<sub>6</sub> hydrocarbylene)(C<sub>3</sub>-C<sub>8</sub> cyclohydrocarbyl), C<sub>3</sub>-C<sub>8</sub> cyclohydrocarbylene)(C<sub>3</sub>-C<sub>8</sub> cyclohydrocarbyl), -(C<sub>1</sub>-C<sub>6</sub> hydrocarbylene)(C<sub>4</sub>-C<sub>8</sub> heterocyclohydrocarbyl), -(C<sub>3</sub>-C<sub>8</sub> cyclohydrocarbylene)(C<sub>4</sub>-C<sub>8</sub> heterocyclohydrocarbyl), or -O-aryl, or -O-(C<sub>1</sub>-C<sub>6</sub> hydrocarbylene)-aryl; wherein said aryl, C<sub>4</sub>-C<sub>8</sub> heterocyclohydrocarbyl, C<sub>1</sub>-C<sub>6</sub> hydrocarbyl, C<sub>3</sub>-C<sub>8</sub> cyclohydrocarbyl, C<sub>3</sub>-C<sub>8</sub> cyclohydrocarbylene, and C<sub>1</sub>-C<sub>6</sub> hydrocarbylene groups may each independently be optionally substituted with from one to six fluoro and may each independently be optionally substituted with one or two substituents  $R_8$  independently selected from the group consisting of C<sub>1</sub>-C<sub>4</sub> hydrocarbyl, -C<sub>3</sub>-C<sub>8</sub> cyclohydrocarbyl, hydroxy, chloro, bromo, iodo, CF<sub>3</sub>, -O-(C<sub>1</sub>-C<sub>6</sub> hydrocarbyl), -O-(C<sub>3</sub>-C<sub>5</sub> cyclohydrocarbyl), -O-CO-(C<sub>1</sub>-C<sub>4</sub> hydrocarbyl), -O-CO-NH(C<sub>1</sub>-C<sub>4</sub> hydrocarbyl), -O-CO-N(R<sub>24</sub>)(R<sub>25</sub>), -N(R<sub>24</sub>)(R<sub>25</sub>), -S(C<sub>1</sub>-C<sub>4</sub> hydrocarbyl), -S(C<sub>3</sub>-C<sub>5</sub> cyclohydrocarbyl) [-]N(C<sub>1</sub>-C<sub>4</sub> hydrocarbyl)CO(C<sub>1</sub>-C<sub>4</sub> hydrocarbyl), -NHCO(C<sub>1</sub>-C<sub>4</sub> hydrocarbyl), -COO(C<sub>1</sub>-C<sub>4</sub> hydrocarbyl), -CONH(C<sub>1</sub>-C<sub>4</sub> hydrocarbyl), -CONC<sub>1</sub>-C<sub>4</sub> hydrocarbyl)(C<sub>1</sub>-C<sub>2</sub> hydrocarbyl), CN, NO<sub>2</sub>, -OSO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub> hydrocarbyl), S<sup>+</sup>(C<sub>1</sub>-C<sub>6</sub> hydrocarbyl)(C<sub>1</sub>-C<sub>2</sub> hydrocarbyl) I<sup>-</sup>, -SO(C<sub>1</sub>-C<sub>4</sub> hydrocarbyl) and -SO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub> hydrocarbyl); and wherein the C<sub>1</sub>-C<sub>6</sub> hydrocarbyl, C<sub>1</sub>-C<sub>6</sub> hydrocarbylene, C<sub>3</sub>-C<sub>8</sub> cyclohydrocarbyl, C<sub>3</sub>-C<sub>8</sub> cyclohydrocarbylene, and C<sub>3</sub>-C<sub>8</sub> heterocyclohydrocarbyl moieties of  $R_1$  may optionally independently contain from



one to three double or triple bonds; and wherein the C<sub>1</sub>-C<sub>4</sub> hydrocarbyl moieties and C<sub>1</sub>-C<sub>6</sub> hydrocarbyl moieties of R<sub>8</sub> can optionally independently be substituted with hydroxy, amino, C<sub>1</sub>-C<sub>4</sub> alkyl, aryl, -CH<sub>2</sub>-aryl, C<sub>3</sub>-C<sub>5</sub> cycloalkyl, or -O-(C<sub>1</sub>-C<sub>4</sub> alkyl), and can optionally independently be substituted with from one to six fluoro, and can optionally contain one or two double or triple bonds; and wherein each heterocyclohydrocarbyl group of R<sub>1</sub> contains from one to three heteromoiety selected from oxygen, S(O)<sub>m</sub>, nitrogen, and NR<sub>12</sub>;

R<sub>2</sub> is hydrogen, C<sub>1</sub>-C<sub>12</sub> hydrocarbyl, C<sub>3</sub>-C<sub>8</sub> cyclohydrocarbyl, C<sub>4</sub>-C<sub>8</sub> heterocyclohydrocarbyl, -(C<sub>1</sub>-C<sub>6</sub> hydrocarbylene)(C<sub>3</sub>-C<sub>8</sub> cyclohydrocarbyl), -(C<sub>3</sub>-C<sub>8</sub> cyclohydrocarbylene)(C<sub>3</sub>-C<sub>8</sub> cyclohydrocarbyl), -(C<sub>1</sub>-C<sub>6</sub> hydrocarbylene)(C<sub>4</sub>-C<sub>8</sub> heterocyclohydrocarbyl), -(C<sub>3</sub>-C<sub>6</sub> cyclohydrocarbylene)(C<sub>4</sub>-C<sub>8</sub> heterocyclohydrocarbyl), aryl, -(C<sub>1</sub>-C<sub>6</sub> hydrocarbylene)aryl, or -(C<sub>3</sub>-C<sub>8</sub> cyclohydrocarbylene)(aryl); wherein each of the foregoing R<sub>2</sub> groups may optionally be substituted with from one to three substituents independently selected from chloro, fluoro, and C<sub>1</sub>-C<sub>6</sub> alkyl, wherein one of said one to three substituents can further be selected from bromo, iodo, C<sub>1</sub>-C<sub>6</sub> alkoxy, -OH, -O-CO-(C<sub>1</sub>-C<sub>6</sub> alkyl), -O-CO-N(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl), -S (C<sub>1</sub>-C<sub>6</sub> alkyl), -S(O)(C<sub>1</sub>-C<sub>6</sub> alkyl), -S(O)<sub>2</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), S<sup>+</sup>(C<sub>1</sub>-C<sub>6</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl)I<sup>-</sup>, CN, and NO<sub>2</sub>; and wherein the C<sub>1</sub>-C<sub>12</sub> hydrocarbyl, -(C<sub>1</sub>-C<sub>6</sub> hydrocarbylene), and cyclohydrocarbyl groups of 5 - 8 carbon atoms, cyclohydrocarbylene groups of 5 to 8 carbon atoms and heterocyclohydrocarbyl groups of 5 to 8 atoms of R<sub>2</sub> may optionally independently contain from one to three double or triple bonds; and wherein each heterocyclohydrocarbyl group of R<sub>2</sub> contains



from one to three heteromoieties selected from oxygen,  $S(O)_m$ , nitrogen, and  $NR_{12}$ ;

or when  $R_1$  and  $R_2$  are as in  $-NHCHR_1R_2$ ,  $-OCHR_1R_2$ ,  $-SCHR_1R_2$ ,  $-CHR_1R_2$  or  $-NR_1R_2$ ,

$R_1$  and  $R_2$  of B may form a saturated 5- to 8-membered ring which may optionally contain one or

two double bonds and in which one or two of the ring carbons may optionally be replaced by an

oxygen,  $S(O)_m$ , nitrogen or  $NR_{12}$ ; and which carbocyclic ring can optionally be substituted with

from 1 to 3 substituents selected from the group consisting of hydroxy,  $C_1$ - $C_4$  alkyl, fluoro, chloro, bromo, iodo,  $CF_3$ ,  $-O-(C_1-C_4 \text{ alkyl})$ ,  $-O-CO-(C_1-C_4 \text{ alkyl})$ ,

$-O-CO-NH(C_1-C_4 \text{ alkyl})$ ,  $-O-CO-N(C_1-C_4 \text{ alkyl})(C_1-C_2 \text{ alkyl})$ ,  $-NH(C_1-C_4 \text{ alkyl})$ ,

$-N(C_1-C_2 \text{ alkyl})(C_1-C_4 \text{ alkyl})$ ,  $-S(C_1-C_4 \text{ alkyl})$ ,  $-N(C_1-C_4 \text{ alkyl})CO(C_1-C_4 \text{ alkyl})$ ,

$-NHCO(C_1-C_4 \text{ alkyl})$ ,  $-COO(C_1-C_4 \text{ alkyl})$ ,  $-CONH(C_1-C_4 \text{ alkyl})$ ,  $-CON(C_1-C_4$

$alkyl)(C_1-C_2 \text{ alkyl})$ ,  $CN$ ,  $NO_2$ ,  $-OSO_2(C_1-C_4 \text{ alkyl})$ ,  $-SO(C_1-C_4 \text{ alkyl})$ , and  $-SO(C_1-C_4$

$alkyl)$ , wherein one of said one to three substituents can further be selected from phenyl;

$R_3$  is methyl, ethyl, fluoro, chloro, bromo, iodo, cyano, methoxy,  $OCF_3$ ,  $NH_2$ ,  $NH(C_1-C_2 \text{ alkyl})$ ,  $N(CH_3)_2$ ,  $-NHCOCF_3$ ,  $-NHCH_2CF_3$ ,  $S(O)_m(C_1-C_4 \text{ alkyl})$ ,  $CONH_2$ ,  $-CONHCH_3$ ,  $CON(CH_3)_2$ ,  $-CF_3$ , or  $CH_2OCH_3$ ;

$R_4$  is hydrogen,  $C_1$ - $C_4$  hydrocarbyl,  $C_3$ - $C_5$  cycloalkyl,  $-(C_1-C_4 \text{ hydrocarbylene})(C_3-C_5 \text{ cycloalkyl})$ ,  $-(C_3-C_5 \text{ cycloalkylene})(C_3-C_6 \text{ cycloalkyl})$ , cyano, fluoro, chloro, bromo, iodo,  $-OR_{24}$   $C_1$ - $C_6$  alkoxy,  $-O-$  cycloalkyl,  $-O-(C_1-C_4$



hydrocarbylene)(C<sub>3</sub>-C<sub>5</sub> cycloalkyl), -O-(C<sub>3</sub>-C<sub>5</sub> cycloalkylene)(C<sub>3</sub>-C<sub>5</sub> cycloalkyl), -CH<sub>2</sub>SC(S)O(C<sub>1</sub>-C<sub>4</sub> alkyl), CH<sub>2</sub>OCF<sub>3</sub>, CF<sub>3</sub>, amino, nitro, -NR<sub>24</sub>R<sub>25</sub>, -(C<sub>1</sub>-C<sub>4</sub> hydrocarbylene)-OR<sub>24</sub>, -(C<sub>1</sub>-C<sub>4</sub> hydrocarbylene)Cl, -(C<sub>1</sub>-C<sub>4</sub> hydrocarbylene)NR<sub>24</sub>R<sub>25</sub>, -NHCOR<sub>24</sub>, -NHCONR<sub>24</sub>R<sub>25</sub>, -CH=NOR<sub>24</sub>, -NHNOR<sub>24</sub>R<sub>25</sub>, -S(O)<sub>m</sub>R<sub>24</sub>, -C(O)R<sub>24</sub>, -OC(O)R<sub>24</sub>, -C(O)CN, -C(O)NR<sub>24</sub>R<sub>25</sub>, -C(O)NHNOR<sub>24</sub>R<sub>25</sub>, and -COOR<sub>24</sub>, wherein the hydrocarbyl and hydrocarbylene groups of R<sub>4</sub> may optionally independently contain one or two double or triple bonds and may optionally independently be substituted with one or two substituents R<sub>10</sub> independently selected from hydroxy, amino, -NHCOCH<sub>3</sub>, -NHCOCH<sub>2</sub>Cl, -NH(C<sub>1</sub>-C<sub>2</sub> alkyl), -N(C<sub>1</sub>-C<sub>2</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub>alkyl), -COO(C<sub>1</sub>-C<sub>4</sub> alkyl), -COOH, -CO(C<sub>1</sub>-C<sub>4</sub> alkyl), C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>1</sub>-C<sub>3</sub> thioalkyl, cyano and nitro, and with one to four substituents independently selected from fluoro and chloro;

R<sub>5</sub> is aryl or heteroaryl and is substituted with from one to four substituents R<sub>27</sub> independently selected from halo, C<sub>1</sub>-C<sub>10</sub> hydrocarbyl, -(C<sub>1</sub>-C<sub>4</sub> hydrocarbylene)(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), -(C<sub>1</sub>-C<sub>4</sub> hydrocarbylene)(C<sub>4</sub>-C<sub>8</sub> heterocycloalkyl), -(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), -(C<sub>4</sub>-C<sub>8</sub> heterocycloalkyl), -(C<sub>3</sub>-C<sub>8</sub> cycloalkylene)(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), -(C<sub>3</sub>-C<sub>8</sub> cycloalkylene)(C<sub>4</sub>-C<sub>8</sub> heterocycloalkyl), C<sub>1</sub>-C<sub>4</sub> haloalkyl, C<sub>1</sub>-C<sub>4</sub> haloalkoxy, nitro, cyano, -NR<sub>24</sub>R<sub>25</sub>, -NR<sub>24</sub>COR<sub>25</sub>, -NR<sub>24</sub>CO<sub>2</sub>R<sub>26</sub>, -COR<sub>24</sub>, -OR<sub>25</sub>, -CONR<sub>24</sub>R<sub>25</sub>, -CON(OR<sub>22</sub>)R<sub>23</sub>, -CO<sub>2</sub>R<sub>26</sub>, -C=N(OR<sub>22</sub>)R<sub>23</sub>, and -S(O)<sub>m</sub>R<sub>23</sub>; wherein said C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, (C<sub>1</sub>-C<sub>4</sub> hydrocarbylene), (C<sub>3</sub>-C<sub>8</sub> cycloalkyl), (C<sub>3</sub>-C<sub>8</sub> cycloalkylene), and (C<sub>4</sub>-C<sub>8</sub> heterocycloalkyl) groups can be optionally substituted with from one to three substituents independently selected from C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, (C<sub>1</sub>-C<sub>4</sub> hydrocarbylene)(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), -(C<sub>3</sub>-C<sub>8</sub> cycloalkylene)(C<sub>3</sub>-C<sub>8</sub>



cycloalkyl), C<sub>1</sub>-C<sub>4</sub> haloalkyl, hydroxy, C<sub>1</sub>-C<sub>6</sub> alkoxy, nitro, halo, cyano, -NR<sub>24</sub>R<sub>25</sub>, -NR<sub>24</sub>COR<sub>25</sub>, NR<sub>24</sub>CO<sub>2</sub>R<sub>26</sub>, -COR<sub>24</sub>, -OR<sub>25</sub>, -CONR<sub>24</sub>R<sub>25</sub>, CO<sub>2</sub>R<sub>26</sub>, -CO(NOR<sub>22</sub>)R<sub>25</sub>, and -S(O)<sub>m</sub>R<sub>23</sub>; and wherein two adjacent substituents of the R<sub>5</sub> group can optionally form a 5-7 membered ring, saturated or unsaturated, fused to R<sub>5</sub>, which ring optionally can contain one, two, or three heterologous members independently selected from O, S(O)<sub>m</sub>, and N, but not any -S-S-, -O-O-, -S-O-, or -N-S- bonds, and which ring is optionally substituted with C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, -(C<sub>1</sub>-C<sub>4</sub> alkylene)(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), -(C<sub>3</sub>-C<sub>8</sub> cycloalkylene)(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), C<sub>1</sub>-C<sub>4</sub> haloalkyl, nitro, halo, cyano -NR<sub>24</sub>R<sub>25</sub>, NR<sub>24</sub>COR<sub>25</sub>, NR<sub>24</sub>CO<sub>2</sub>R<sub>26</sub>, -COR<sub>24</sub>, -OR<sub>25</sub>, -CONR<sub>24</sub>R<sub>25</sub>, CO<sub>2</sub>R<sub>26</sub>, -CO(NOR<sub>26</sub>)R<sub>25</sub>, or -S(O)<sub>m</sub>R<sub>23</sub>; wherein one of said one to four optional substituents R<sub>27</sub>, can further be selected from -SO<sub>2</sub>NH(C<sub>1</sub>-C<sub>4</sub> alkyl), -SO<sub>2</sub>NH(C<sub>1</sub>-C<sub>4</sub> alkylene)(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), SO<sub>2</sub>NH(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), -SO<sub>2</sub>NH(C<sub>3</sub>-C<sub>8</sub> cycloalkylene)(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), -SO<sub>2</sub>N(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl), -SO<sub>2</sub>NH<sub>2</sub>, -NHSO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub> alkyl), -NHSO<sub>2</sub>(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), -NHSO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub> alkylene)(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), and -NHSO<sub>2</sub>(C<sub>3</sub>-C<sub>8</sub> cycloalkylene)(C<sub>3</sub>-C<sub>8</sub> cycloalkyl); and wherein the hydrocarbyl, and hydrocarbylene groups of R<sub>5</sub> may independently optionally contain one double or triple bond;

R<sub>6</sub> is hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, -(C<sub>1</sub>-C<sub>6</sub> alkylene)(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), or -(C<sub>3</sub>-C<sub>8</sub> cycloalkylene)(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), wherein said alkyl and cycloalkyl may optionally be substituted with one hydroxy, methoxy, ethoxy or fluoro group;

or R<sub>6</sub> and R<sub>4</sub> can together form an oxo (=O) group, or can be connected to form a 3-8



membered carbocyclic ring, optionally containing one to three double bonds, and optionally containing one, two, or three heterologous ring members selected from O, SO<sub>m</sub>, N, and NR<sub>12</sub>, but not containing any -O-O-, -S-O-, -S-S-, or -N-S- bonds, and further optionally substituted with C<sub>1</sub>-C<sub>4</sub> hydrocarbyl or C<sub>3</sub>-C<sub>6</sub> cycloalkyl, wherein said C<sub>1</sub>-C<sub>4</sub> hydrocarbyl substituent may optionally contain one double or triple bond;

R<sub>7</sub> is hydrogen, methyl, fluoro, chloro, bromo, iodo, cyano, hydroxy, -O(C<sub>1</sub>-C<sub>2</sub>)alkyl, -O(cyclopropyl), -COO(C<sub>1</sub>-C<sub>2</sub> alkyl), -COO(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), -OCF<sub>3</sub>, -CF<sub>3</sub>, -CH<sub>2</sub>OH or CH<sub>2</sub>OCH<sub>3</sub>;

R<sub>11</sub> is hydrogen, hydroxy, fluoro, ethoxy, or methoxy;

R<sub>12</sub> is hydrogen or C<sub>1</sub>-C<sub>4</sub> alkyl;

R<sub>22</sub> is independently at each occurrence selected from hydrogen, C<sub>1</sub>-C<sub>14</sub> alkyl, C<sub>1</sub>-C<sub>14</sub> haloalkyl, C<sub>3</sub>-C<sub>6</sub> alkenyl, C<sub>3</sub>-C<sub>6</sub> alkynyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, (C<sub>3</sub>-C<sub>8</sub> cycloalkylene)(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), and (C<sub>1</sub>-C<sub>4</sub>) alkylene)(C<sub>3</sub>-C<sub>8</sub> cycloalkyl);

R<sub>23</sub> is independently at each occurrence selected from C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> haloalkyl, C<sub>2</sub>-C<sub>8</sub> alkoxyalkyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, -(C<sub>1</sub>-C<sub>4</sub> alkylene)(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), -(C<sub>3</sub>-C<sub>8</sub> cycloalkylene)(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), aryl, -(C<sub>1</sub>-C<sub>4</sub> alkylene)aryl, piperidine, pyrrolidine, piperazine, N-methylpiperazine, morpholine, and thiomorpholine;

R<sub>24</sub> and R<sub>25</sub> are independently at each occurrence selected from hydrogen, -C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> haloalkyl, -(C<sub>1</sub>-C<sub>4</sub> alkylene)OH, -(C<sub>1</sub>-C<sub>4</sub> alkylene)-O-(C<sub>1</sub>-C<sub>4</sub> alkyl), -(C<sub>1</sub>-C<sub>4</sub> alkylene)-O-(C<sub>3</sub>-C<sub>5</sub> cycloalkyl), C<sub>3</sub>-C<sub>8</sub> cycloalkyl, -(C<sub>1</sub>-C<sub>4</sub> alkylene)(C<sub>3</sub>-C<sub>8</sub>



cycloalkyl), -(C<sub>3</sub>-C<sub>8</sub> cycloalkylene)(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), -C<sub>4</sub>-C<sub>8</sub> heterocyclohydrocarbyl, -(C<sub>1</sub>-C<sub>4</sub> alkylene)(C<sub>4</sub>-C<sub>8</sub> heterocyclohydrocarbyl), -(C<sub>3</sub>-C<sub>8</sub> cycloalkylene)(C<sub>4</sub>-C<sub>8</sub> heterocyclohydrocarbyl), aryl, and -(C<sub>1</sub>-C<sub>4</sub> alkylene)(aryl), wherein the -C<sub>4</sub>-C<sub>8</sub> heterocyclohydrocarbyl groups can each independently optionally be substituted with aryl, CH<sub>2</sub>-aryl, or C<sub>1</sub>-C<sub>4</sub> alkyl, and can optionally contain one or two double or triple bonds; or, when R<sub>24</sub> and R<sub>25</sub> are as NR<sub>24</sub>R<sub>25</sub>, -C(O)NR<sub>24</sub>R<sub>25</sub>, -(C<sub>1</sub>-C<sub>4</sub> alkylene)NR<sub>24</sub>R<sub>25</sub>, or -NHCONR<sub>24</sub>R<sub>25</sub>, then NR<sub>24</sub>R<sub>25</sub> may further optionally form a 4 to 8 membered heterocyclic ring optionally containing one or two further hetero members independently selected from S(O)<sub>m</sub>, oxygen, nitrogen, and NR<sub>12</sub>, and optionally containing from one to three double bonds;

R<sub>26</sub> is independently at each occurrence selected from C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> haloalkyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, -(C<sub>1</sub>-C<sub>4</sub> alkylene)(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), -(C<sub>3</sub>-C<sub>8</sub> cycloalkylene)(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), aryl, and -(C<sub>1</sub>-C<sub>4</sub> alkylene)(aryl); and

wherein each m is independently zero, one, or two,

with the proviso that heterocyclohydrocarbylene groups of the compound of formula I, do not comprise any -S-S-, -S-O-, -N-S-, or -O-O- bonds, and do not comprise more than two oxygen or S(O)<sub>m</sub> heterologous members.

Claims 2, 3 and 4 (cancelled)

Claim 5 (currently amended) A compound according to claim 2, wherein R<sub>2</sub> is C<sub>1</sub>-C<sub>4</sub> alkyl which may optionally be substituted by fluoro, chloro, CF<sub>3</sub>, C<sub>1</sub>-C<sub>4</sub> alkyl or C<sub>1</sub>-C<sub>4</sub> alkoxy.



Claim 6 (currently amended) A compound according to claim 2 1, wherein R<sub>3</sub> is methyl, chloro, or methoxy.

Claim 7 (currently amended) A compound according to claim 2 1, wherein R<sub>4</sub> is methyl, -CH<sub>2</sub>OH, cyano, trifluoromethoxy, methoxy, chloro, trifluoromethyl, -COOCH<sub>3</sub>, -CH<sub>2</sub>OCH<sub>3</sub>, -CH<sub>2</sub>Cl, -CH<sub>2</sub>F, ethyl, amino or nitro.

Claim 8 (currently amended) A compound according to claim 2 1, wherein R<sub>5</sub> is phenyl substituted with two or three substituents.

Claim 9 (currently amended) A compound according to claim 2 1, wherein R<sub>5</sub> is pyridyl substituted with two or three substituents.

Claim 10 (original) A compound according to claim 8 wherein said substituents are selected, independently, from fluoro, chloro, bromo, iodo, C<sub>1</sub>-C<sub>4</sub> alkoxy, trifluoromethyl, C<sub>1</sub>-C<sub>6</sub> alkyl which may optionally be substituted with one hydroxy, C<sub>1</sub>-C<sub>4</sub> alkoxy or fluoro group and which may optionally contain one carbon-carbon double or triple bond, -(C<sub>1</sub>-C<sub>4</sub> alkylene)O(C<sub>1</sub>-C<sub>2</sub> alkyl), C<sub>1</sub>-C<sub>3</sub> hydroxyalkyl, hydroxy, formyl, COO(C<sub>1</sub>-C<sub>2</sub> alkyl), -(C<sub>1</sub>-C<sub>2</sub> alkylene)amino, and -(C(O)(C<sub>1</sub>-C<sub>4</sub> alkyl).

Claim 11 (original) A compound according to claim 9 wherein said substituents are selected, independently, from fluoro, chloro, bromo, iodo, C<sub>1</sub>-C<sub>4</sub> alkoxy, trifluoromethyl, C<sub>1</sub>-C<sub>6</sub> alkyl which may optionally be substituted with one hydroxy,



C<sub>1</sub>-C<sub>4</sub> alkoxy or fluoro group and which may optionally contain one carbon-carbon double or triple bond, -(C<sub>1</sub>-C<sub>4</sub> alkylene)O(C<sub>1</sub>-C<sub>2</sub> alkyl), C<sub>1</sub>-C<sub>3</sub> hydroxyalkyl, hydroxy, formyl, -COO(C<sub>1</sub>-C<sub>2</sub> alkyl), -(C<sub>1</sub>-C<sub>2</sub> alkylene)amino and -(C(O)(C<sub>1</sub>-C<sub>4</sub> alkyl).

Claim 12 (previously presented) A compound according to claim 1, wherein said compound is selected from the group consisting of:

[3,6-dimethyl-2-(2,4,6-trimethyl-phenoxy)-pyridin-4-yl]-diethyl-amine;  
[3,6-dimethyl-2-(2,4,6-trimethyl-phenoxy)-pyridin-4-yl]-ethyl-propyl-amine;  
butyl-[3,6-dimethyl-2-(2,4,6-trimethyl-phenoxy)-pyridin-4-yl]-ethyl-amine;  
4-(1-ethyl-propoxy)-3,6-dimethyl-2-(2,4,6-trimethyl-phenylsulfanyl)-pyridine;  
butyl-[2-(4-chloro-2,6-dimethyl-phenoxy)-3,6-dimethyl-pyridin-4-yl]-ethyl-amine;  
[3,6-dimethyl-[2-(2,4,6-trimethyl-phenylsulfanyl)-pyridin-4-yl]-ethyl-propyl-amine;  
[2-(4-chloro-2,6-dimethyl-phenoxy)-3,6-dimethyl-pyridin-4-yl]-ethyl-propyl-amine;  
N<sub>4</sub>-(1-ethyl-propyl)-6-methyl-3-nitro-N<sub>2</sub>-(2,4,6-trimethyl-phenyl)-pyridine-2,4-diamine;  
3,6-dimethyl-2-(2,4,6-trimethyl-phenoxy)-pyridin-4-yl]-ethyl-(2,2,2-trifluoro-ethyl)-amine;  
N<sub>4</sub>-(1-ethyl-propyl)-6-methyl-N<sub>2</sub>-(2,4,6-trimethyl-phenyl)-pyridine-2,3,4-triamine;  
(N-(1-ethyl-propyl)-2-methyl-5-nitro-N'-(2,4,6-trimethyl-pyridin-3-yl)-pyrimidine-4,6-diamine;  
[2-(4-chloro-2,6-dimethyl-phenoxy)-3,6-dimethyl-pyridin-4-yl]-diethyl-amine;  
(1-ethyl-propyl)-[5-methyl-3-(2,4,6-trimethyl-phenyl)-3H-imidazo [4,5-b]pyridin-7-



yl-amine;

[2,5-dimethyl-3-(2,4,6-trimethyl-phenyl)-3H-imidazo[4,5-b]pyridin-4-yl]-(1-ethyl-propyl)- amine;

[4-(1-ethyl-propoxy)-3,6-dimethyl-pyridin-2-yl]-(2,4,6-trimethylphenyl)-amine;

[4-(1-ethyl-propoxy)-3,6-dimethyl-2-(2,4,6-trimethylphenoxy)-pyridine;

[3,6-dimethyl-2-(2,4,6-trimethyl-phenoxy)-pyridin-4-yl]-(1-ethyl-propyl)-amine; and

[2-(4-chloro-2,6-dimethyl-phenoxy)-3,6-dimethyl-pyridin-4-yl]-(1-ethyl-propyl)-amine or pharmaceutically acceptable salt of one of the above compounds.

Claim 13 (previously presented) A pharmaceutical composition for the treatment of (a) a disorder or condition the treatment of which can be effected or facilitated by antagonizing CRF or (b) a disorder or condition selected from inflammatory disorders, pain, asthma, psoriasis and allergies; generalized anxiety disorder; panic; phobias; obsessive-compulsive disorder; post-traumatic stress disorder; sleep disorders induced by stress; pain perception; mood disorders, mood disorders associated with premenstrual syndrome, and postpartum depression; dysthemia; bipolar disorders; cyclothymia; chronic fatigue syndrome; stress-induced headache; cancer; irritable bowel syndrome, Crohn's disease; spastic colon; post operative ileus; ulcer; diarrhea; stress-induced fever; human immunodeficiency virus infections; neurodegenerative diseases; gastrointestinal diseases; eating disorder; hemorrhagic stress; chemical dependencies or addictions; drug or alcohol withdrawal symptoms; stress-induced psychotic episodes; euthyroid sick syndrome; syndrome of inappropriate antidiuretic hormone; obesity; infertility; head trauma; spinal cord trauma; ischemic neuronal



damage; excitotoxic neuronal damage; stroke; immune dysfunctions; muscular spasms; urinary incontinence; senile dementia of the Alzheimer's type; multi infarct dementia; amyotrophic lateral sclerosis; hypertension; tachycardia; congestive heart failure; osteoporosis; premature birth; hypoglycemia, and Syndrome X in a mammal or bird, comprising an amount of a compound according to claim 1 that is effective in the treatment of such disorder or condition, and a pharmaceutically acceptable carrier.

Claim 14 (previously presented) A pharmaceutical composition according to claim 13 for the treatment of a disorder selected from inflammatory disorders; pain, asthma, psoriasis and allergies; generalized anxiety disorder; panic; phobias; obsessive compulsive disorder; post-traumatic stress disorder; sleep disorders induced by stress; pain perception; mood disorders; dysthemia; bipolar disorders; cyclothymia; fatigue syndrome; stress induced headache; cancer; irritable bowel syndrome, Crohn's disease; spastic colon; human immunodeficiency virus (HIV) infections; neurodegenerative diseases; gastrointestinal diseases; eating disorders; chemical dependencies and addictions; obesity; infertility; head traumas; spinal cord trauma; ischemic neuronal damage; excitotoxic neuronal damage; epilepsy; stroke; immune dysfunctions; muscular spasms; urinary incontinence; senile dementia of the Alzheimer's type; multi infarct dementia; amyotrophic lateral sclerosis; and hypoglycemia in a mammal.

Claim 15 (withdrawn) A method for the treatment of (a) a disorder or condition the treatment of which can be effected or facilitated by antagonizing CRF, including but



not limited to disorders induced or facilitated by CRF, or (b) a disorder or condition selected from inflammatory disorders such as rheumatoid arthritis and osteoarthritis, pain, asthma, psoriasis and allergies; generalized anxiety disorder; panic; phobias, including social phobia, agoraphobia, and specific phobias; obsessive-compulsive disorder; post-traumatic stress disorder; sleep disorders induced by stress; pain perception such as fibromyalgia; mood disorders such as depression, including major depression, single episode depression, recurrent depression, child abuse induced depression, mood disorders associated with premenstrual syndrome, and postpartum depression; dysthymia; bipolar disorders; cyclothymia; chronic fatigue syndrome; stress-induced headache; cancer; irritable bowel syndrome, Crohn's disease; spastic colon; post operative ileus; ulcer; diarrhea; stress-induced fever; human immunodeficiency virus infections; neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease and Huntington's disease; gastrointestinal diseases; eating disorders such as anorexia and bulimia nervosa; hemorrhagic stress; chemical dependencies or addictions, including dependencies or addictions to alcohol, cocaine, heroin, benzodiazapines, or other drugs; drug or alcohol withdrawal symptoms; stress-induced psychotic episodes; euthyroid sick syndrome; syndrome of inappropriate antidiuretic hormone; obesity; infertility; head trauma; spinal cord trauma; ischemic neuronal damage, including cerebral ischemia, for example cerebral hippocampal ischemia; excitotoxic neuronal damage; epilepsy; stroke; immune dysfunctions including stress induced immune dysfunctions, including porcine stress syndrome, bovine shipping fever, equine paroxysmal fibrillation, confinement dysfunction in chicken, sheering stress in sheep, and human-animal interaction stress in dogs;



muscular spasms; urinary incontinence; senile dementia of the Alzheimer's type; multiinfarct dementia; amyotrophic lateral sclerosis; hypertension; tachycardia; congestive heart failure; osteoporosis; premature birth; hypoglycemia, and Syndrome X in a mammal or bird, comprising administering to a subject in need of said treatment an amount of a compound according to claim 1, that is effective in treating such disorder or condition.

Claims 16-28 (cancelled)

Claim 29 (previously presented) A compound as claimed in claim 1 wherein  $R_{24}$  and  $R_{25}$  are selected from  $-CF_3$ ,  $-CHF_2$ ,  $CF_2CF_3$ , and  $CH_2CF_3$ ,

Claim 30 (previously presented) A pharmaceutical composition as claimed in claim 13 for treatment of a mood disorder selected from the group consisting of rheumatoid arthritis and osteoarthritis, pain, asthma, psoriasis and allergies.

Claim 31 (previously presented) A pharmaceutical composition as claimed in claim 13 for treatment of an inflammatory disorder selected from the group consisting of rheumatoid arthritis and osteoarthritis.

Claim 32 (previously presented) A pharmaceutical composition as claimed in claim 14 for treatment of depression, selected from the group consisting of major depression, single episode depression, recurrent depression, and child abuse induced



depression.

Claim 33 (previously presented) A pharmaceutical composition as claimed in claim 14 for treatment of neurodegenerative diseases selected from the group consisting of Alzheimer's disease, Parkinson's disease and Huntington's disease.

Claim 34 (previously presented) A pharmaceutical composition as claimed in claim 14 for treatment of chemical dependencies or addictions, selected from the group consisting of dependencies or addictions to alcohol, cocaine, heroin, benzodiazapines, or other drugs.

Claim 35 (previously presented) A pharmaceutical composition as claimed in claim 14 for treatment of cerebral ischemia.

Claim 36 (previously presented) A pharmaceutical composition as claimed in claim 14 for treatment of stress induced immune dysfunctions selected from the group consisting of porcine stress syndrome, bovine shipping fever, equine paroxysmal fibrillation, confinement dysfunction in chicken, sheering stress in sheep, and human animal interaction stress in dogs.

Claim 37 (previously presented) A pharmaceutical composition as claimed in claim 14 for treatment of fibromyalgia.



Claim 38 (previously presented) A pharmaceutical composition as claimed in claim 14 for treatment of anorexia or bulimia nervosa.

Claim 39 (previously presented) A pharmaceutical composition as claimed in claim 44 for treatment of cerebral ischemia selected from cerebral hippocampal ischemia.

Claim 40 (previously presented) A pharmaceutical composition as claimed in claim 14 for treatment of including social phobia, agoraphobia or specific phobias.

Claim 41 (previously presented) The pharmaceutical composition according to claim 13 wherein the pain perception is fibromyalgia.

Claim 42 (previously presented) The pharmaceutical composition according to claim 13 wherein the ischemic neuronal damage is cerebral ischemia.

Claim 43 (previously presented) The pharmaceutical composition according to claim 14 wherein mood disorder is depression or postpartum depression.

Claim 44 (previously presented) The pharmaceutical composition according to claim 14 wherein the ischemic neuronal damage is cerebral ischemia.

Claim 45 (previously presented) The pharmaceutical composition according to claim 14 wherein the mammal is a human.



Claim 46 (new). A compound according to claim 12, wherein the compound is the mesylate salt of 4-(1-ethyl-propoxy)-3,6-dimethyl-2-(2,4,6-trimethyl-phenoxy)-pyridine.

Claim 47 (new). A compound according to claim 12, wherein the pharmaceutically acceptable salt is a salt of methanesulfonic acid.